REMARKS

I. Amendments

In the claims, claims 17-20 are canceled, and new claims 21-25 are added. The newly added claims do not constitute new matter and are completely supported throughout the specification and originally filed claims. More particularly, newly added claims 21-25, drawn to a transgenic mouse whose genome comprises a disruption in a serine protease gene comprising SEQ ID NO:1 and a method of producing said mouse can be found, for example, at page 11, line 18 through page 16, line 2, and at page 51, line 22 through page 52, line 2, of the specification.

The foregoing amendments are made solely to expedite prosecution of the application and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. Applicants reserve the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 21-25 are pending in the instant application.

II. Rejections

A. *Rejection under 35 U.S.C. § 101*

The Examiner has rejected claim 19 under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by either a specific asserted utility, a credible asserted utility or a well-established utility.

Claim 19 is drawn to a cell or tissue derived from a transgenic mouse whose genome comprises a heterozygous disruption in an endogenous serine protease, wherein the transgenic mouse, upon breeding with another transgenic mouse whose genome comprises a heterozygous disruption in an endogenous serine protease gene, produces a transgenic mouse having a homozygous disruption in the endogenous serine protease gene which exhibits a developmental abnormality during embryonic development.

The Examiner alleges that the claimed cell or tissue is not supported by a specific asserted utility because the specification does not assert a utility for the cell or tissue. Further, the Examiner states that the cell or tissue is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. The Examiner admits that

the claimed cell or tissue may be utilized to study serine protease gene function in individual developmental pathways, but asserts that the need for such research clearly indicates that the cell or tissue and its function are not disclosed as to a currently available or substantial utility.

Applicants respectfully traverse the rejection. However, Applicants have cancelled claim 19. In view of the cancellation of claim 19, the rejection under 35 U.S.C. § 101 is no longer relevant. Therefore, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 101.

B. Rejection under 35 U.S.C. § 112, first paragraph

1. Claim 19

Claim 19 was also rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth above in the rejection under 35 U.S.C. § 101. Applicants respectfully traverse the rejection. However, in light of the cancellation of claim 19, the rejection under 35 U.S.C. § 112, first paragraph, is no longer relevant, and Applicants request its withdrawal.

2. Claims 17-18 and 20

Claims 17-18 and 20 were rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

According to the Examiner, the claims are readable on a genus of a transgenic mouse comprising a disruption in an endogenous serine protease gene, wherein the transgenic mouse, upon breeding with another transgenic mouse whose genome comprises a heterozygous disruption in an endogenous serine protease gene, produces a transgenic mouse having a homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality during embryonic development. The Examiner asserts that the genus of such a transgenic mouse is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made.

Applicants respectfully traverse the rejection. Applicants contend that a person skilled in the art of gene targeting would be well apprised of how to design a targeting vector which would create a disruption in a serine protease gene as defined by the instant specification and claimed in the present invention. However, Applicants have cancelled claims 17-18 and 20. In light of the

cancellation of claims, the rejection under 35 U.S.C. § 112, first paragraph, is no longer relevant, and Applicants request withdrawal of the rejection.

3. Claims 17-18 and 20

Claims 17-18 and 20 have also been rejected by the Examiner under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for producing a transgenic mouse whose genome comprises a heterozygous disruption in the serine protease gene set forth in SEQ ID NO:1 and breeding the mouse with a transgenic mouse with the same disruption to produce an embryo that dies between 12.5 and 14.5 days in the uterus, does not reasonably provide enablement for making a transgenic mouse whose genome comprises a disruption in any endogenous serine protease gene and using the mouse to produce a transgenic mouse having a homozygous disruption in an endogenous serine protease and exhibiting any developmental abnormality during embryonic development.

Specifically, the Examiner asserts that the claimed invention is not supported by a sufficient written description to show possession of the genus of a transgenic mouse as claimed, and particularly that one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended (*e.g.* for producing a transgenic mouse having a homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality during embryonic development).

In general, the Examiner concludes that the phenotype of a transgenic mouse comprising a disruption in a serine protease gene, which genes comprise a large family of proteolytic enzymes, would be unpredictable at the time of filing of the instant application. The Examiner asserts that the specification is not enabling for the transgenic mice as claimed, wherein the transgenic mice are used to produce a transgenic mouse having a homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality. Particularly, the Examiner alleges that the specification does not provide sufficient guidance of factual evidence for which endogenous serine protease can be disrupted resulting in the transgenic mouse with the phenotype as claimed.

The Examiner further concludes that the specification does not provide any relevant teachings or sufficient guidance with regard to the production of a representative number of targeting vectors for producing a genus of transgenic mice comprising disruptions in a serine protease gene exhibiting a genus of developmental abnormalities. The Examiner also alleges

that the claimed method is not enabled because it omits the step of introducing a mouse embryonic stem cell into a blastocyst of a pseudopregnant mouse, in view of the art of record. In addition, the Examiner asserts that the claimed method is not enabling for breeding the chimeric mice to produce a transgenic mouse as claimed because it does not disclose breeding two mice, which is considered the status of the art. Finally, the Examiner alleges that the specification does not provide sufficient guidance for the production of the chimeric mouse as is claimed in the method.

The Applicants disagree with the Examiner's conclusions, and respectfully traverse the rejection. In particular, Applicants assert that a serine protease gene has been well defined and described in the instant specification (see page 7 of the specification and Figures 1 and 2), and that the instant specification provides sufficient description of the creation of a transgenic mouse comprising a disruption in the serine protease as defined in the specification and as claimed in the present claims. Applicants believe that they have sufficiently described the production of the transgenic mouse comprising the phenotype as claimed, and in particular a phenotype of a developmental abnormality comprising a lethality. Further, with regard to the method of producing the claimed transgenic mouse, the Examiner has described the state of the art at the time of filing with regard to the claimed method. Applicants contend that the specification in combination with the state of the art of gene targeting discussed by the Examiner would be sufficient guidance for one skilled in this art to produce the present invention as claimed. More particularly, Applicants submit that one skilled in the art of gene targeting would be well aware of the steps necessary to produce the claimed transgenic mouse by the method of producing a transgenic mouse as claimed by the Applicants. Additionally, Applicants contend that for the same reasons, an ordinary artisan would have sufficient guidance, within the instant specification and in the knowledge in the art, to produce the chimeric mouse utilized in the presently claimed method.

For the reasons set forth above, Applicants believe that the rejection of claims 17-18 and 20 under 35 U.S.C. § 112, first paragraph, is improper. However, in order to expedite prosecution of the instant application, Applicants have cancelled claims 17-18 and 20, rendering the rejection moot.

Applicants have submitted new claims 21-25, which are fully enabled by the teachings of the specification and examples provided therein. In light of the cancellation of claims and

submission of new claims, the rejections under 35 U.S.C. § 112, first paragraph, are no longer relevant. Applicants respectfully request withdrawal of the rejection.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-386.

Respectfully submitted,

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